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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,748	08/11/2006	Patrick Gerard Johnston	36290-0415-00-US	1280
23973 7590 01/07/2010 DRINKER BIDDLE & REATH ATTN: INTELLECTUAL PROPERTY GROUP ONE LOGAN SQUARE 18TH AND CHERRY STREETS PHILADELPHIA, PA 19103-6996				
EXAMINER SCHNIZER, RICHARD A				
ART UNIT		PAPER NUMBER		
1635				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/580,748

Applicant(s)

JOHNSTON ET AL.

Examiner

Richard Schnizer

Art Unit

1635

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 December 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15, 29, 30 and 32-52 is/are pending in the application.
- 4a) Of the above claim(s) 1-15, 29, 40, 41, 45 and 46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 30, 32-39, 42-44 and 47-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 May 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-848)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

An amendment was received and entered on 12/18/09.

Claim 31 was canceled.

Claims 1-15, 29, 30, and 32-52 remain pending.

Claims 1-15, 29, 40, 41, 45 and 46 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/10/2008.

Claims 30, 32-39, 42-44 and 47-52 are under consideration.

Rejections/Objections not reiterated are withdrawn.

The rejection of claims 30-39, 42, and 47 is withdrawn in view of Applicant's amendment of these claims to require that a topoisomerase I inhibitor is present when a death receptor binding member is present.

Priority

The instant application is the national phase of PCT/GB2004/005006, filed 11/26/04, and claims priority to GB 0327499.0 and GB 0327493.3, each filed 11/26/03. Neither of the foreign priority documents supports instant SEQ ID NO: 2, which is embraced by all the claims under consideration. Therefore the effective filing date of the instant claims is 11/26/04.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 30, 34, 36-39, 42, 47, and 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siegmund et al (Molecular Medicine 8(11): 725-732, 2002, of record), Wajant et al (US 20040126791), and Xiang et al (Oncogene 21: 3611-3619, 2002).

Siegmund taught that tumor cell sensitivity to TRAIL-induced apoptosis could be enhanced by treatment with siRNA directed to c-FLIP.

Wajant taught compositions and methods for treating TRAIL-resistant cancer cells including treatment with c-FLIP siRNAs, apoptosis inducing drugs, and chemotherapeutics. See abstract, paragraphs 12, 17, 18, 55-58, 64-66, and 72.

Xiang taught that tumor cell sensitivity to TRAIL-induced apoptosis could be enhanced by treatment CPT-11, which is an inhibitor of thymidylate synthase and of topoisomerase I.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the siRNA of Siegmund with the CPT-11 of Xiang in order to form a composition for the treatment of tumors. One would have been motivated to do so in order to obtain the art-recognized benefit of each component in enhancing TRAIL-induced apoptosis of tumor cells. It is prima facie obvious to combine two compositions

each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. See MPEP 2144.06(I).

Regarding claims 36 and 37, the ratio of c-FLIP siRNA and chemotherapeutic agent is considered to be a result effective variable that is routinely optimized by those of ordinary skill.

Regarding claims 38 and 39, absent evidence to the contrary, the extent to which p53 is inactivated and the precise identity of the p53 mutation have no effect on the nature of the claimed composition, and receive no patentable weight.

Regarding claims 42, 51, and 52, it would have been obvious to one of ordinary skill in the art at the time of the invention to organize the siRNA of Siegmund and the CPT-11 of Xiang into a kit because one of skill in the art appreciates that organizing experimental reagents prior to use is standard laboratory practice which reduces the frequency of errors.

Regarding claims 49-52 and the limitation requiring the absence of a death receptor binding member, it would have been obvious to formulate the composition or kit either with or without a death domain binding member (such as TRAIL). This is simply a matter of design choice. On the one hand, it would be simple and efficient to administer all three molecules (siRNA, CPT-11, and TRAIL) in one composition, thereby limiting the number of invasive administrations. On the other hand, one it would also be obvious to administer the siRNA and CPT-11 first in order to place the target tumor cells

in a state in which they are maximally responsive to TRAIL when it is administered separately later. In this case it would have been obvious to make a kit in which the only active ingredients were the siRNA and CPT-11.

Thus the invention as a whole was *prima facie* obvious.

Claims 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hyer et al. (Cancer Biology and Therapy, Vol. 1 (4), pp.401-406, 2001), Uslu et al. (Clin. Cancer Res., Vol. 3(6), pp.963-972, 1997), and Ni et al. (US 20050244857).

The claims are drawn to kits or compositions comprising a c-FLIP inhibitor that is an antisense or RNAi agent, and a chemotherapeutic agent that is a thymidylate synthase inhibitor or a topoisomerase inhibitor.

Hyer taught a method of killing DU145 prostate cancer cells comprising administration of a c-FLIP antisense oligonucleotide and CH11 antibody (see Fig. 5).

Uslu taught the treatment of DU145 prostate cancer cells with chemotherapeutic agents (CDDP (cisplatin), adriamycin and Etoposide) followed by anti-FAS CH-11 treatment resulted in cytotoxicity and apoptosis.

Ni taught a method for treating prostate cancers comprising administering to an individual an antibody that binds to a TRAIL receptor, and a chemotherapeutic agent such as cisplatin (CDDP), oxaliplatin, the thymidylate synthase inhibitor 5-FU, or the topoisomerase inhibitor CPT-11. Ni further suggests explicitly the combination of an antibody, CPT-11, and 5-FU for treatment of conditions that are resistant to individual chemotherapies. See paragraphs 23, 283, 319, 331, 333, 338-341, 347, 352, and 547.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to prepare a composition comprising the c-FLIP antisense and CH11 antibody taught by Hyer, and a chemotherapeutic agent as taught by Uslu or Ni. One would have been motivated to do so in order to obtain the art-recognized benefit of each component in treating tumors. It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. See MPEP 2144.06(I). It would have been obvious to substitute any of chemotherapeutic agents of Ni for those of Uslu or Hyer because cisplatin, oxaliplatin, CPT-11, and 5-FU were all chemotherapeutic agents useful for killing tumor cells.

It would have been obvious to one of ordinary skill in the art at the time of the invention to organize the antisense Hyer and any of the chemotherapeutics of Ni (including CPT-11) into a kit because one of skill in the art appreciates that organizing experimental reagents prior to use is standard laboratory practice which reduces the frequency of errors.

Regarding claims 49-52 and the limitation requiring the absence of a death receptor binding member, it would have been obvious to formulate the composition or kit either with or without a death domain binding member (such as CH-11). This is simply a matter of design choice.

Thus the invention as a whole was *prima facie* obvious.

Claims 30, 32-34, 36-39, 42, and 49-52 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hyer et al. (Cancer Biology and Therapy, Vol. 1 (4), pp.401-406, 2001) and Chatterjee et al (Cancer Res. 61(7148-7154), 2001).

The claims are drawn to a composition comprising a c-FLIP inhibitor, a chemotherapeutic agent, the CH11 antibody, wherein the c-FLIP inhibitor is RNAi comprising either SEQ ID NO:1 or 2.

Hyer taught a method of killing DU145 prostate cancer cells comprising administration of a c-FLIP antisense oligonucleotide and CH11 antibody (see Fig. 5).

Chatterjee taught a method of killing DU-145 prostate cancer cells with the topoisomerase I inhibitor 9-nitrocamptothecin (9NC). 9NC treatment correlated with *de novo* synthesis of Fas (CD 95) and can therefore activate the Fas apoptotic pathway. See abstract.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to prepare a composition comprising the c-FLIP antisense and CH11 antibody taught by Hyer, and the 9NC of Chatterjee. One would have been motivated to do so in order to obtain the art-recognized benefit of each component. It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, e.g. killing tumor cells, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. See MPEP 2144.06(I). Furthermore, one of ordinary skill would expect the use of 9NC

to enhance the effectiveness of CH-11 by increasing the available amount of its receptor, Fas.

Regarding claims 42, 51, and 52, it would have been obvious to one of ordinary skill in the art at the time of the invention to organize the antisense of Hyer and the 9NC of Chatterjee into a kit because one of skill in the art appreciates that organizing experimental reagents prior to use is standard laboratory practice which reduces the frequency of errors.

Regarding claims 49-52 and the limitation requiring the absence of a death receptor binding member, it would have been obvious to formulate the composition or kit either with or without a death domain binding member (such as CH-11). This is simply a matter of design choice. On the one hand, it would be simple and efficient to administer all three molecules (antisense, 9NC, and CH-11) in one composition, thereby limiting the number of invasive administrations. On the other hand, one it would also be obvious to administer the antisense and 9NC first in order to place the target tumor cells in a state in which they are maximally responsive to death receptor stimulation by CH-11 when it is administered separately later.

Thus the invention as a whole was prima facie obvious.

Claims 43, 44, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siegmund et al (Molecular Medicine 8(11): 725-732, 2002), Wajant et al (US 20040126791), and Xiang et al (Oncogene 21: 3611-3619, 2002) as applied to

Siegmund, Wajant, and Xiang can be combined to render obvious a composition comprising CPT-11 and an siRNA directed against c-FLIP.

These references do not teach an siRNA comprising either SEQ ID NO: 1 or SEQ ID NO: 2. Siegmund did teach an siRNA that overlapped with instant SEQ ID NO: 2 by nine nucleotides (underlined):

Instant SEQ ID NO: 1 5'-AAGCAGTCTGTTCAAGGAGCA-3'
Siegmond dsRNA-F2 (908-928 of GenBank U97074) 5'-CAAGGAGCAGGGACAAGTTAC-3'

Tuschl (1) provided extensive teaching on siRNAs their design, and their use in inhibiting a selected target gene. Tuschl taught that siRNA provides enhanced efficacy compared to prior art compounds (paragraph 8, for example). The entire document is directed to the design and use of siRNA.

Tuschl (2) taught that there were ample providers of siRNA in the art at the time of invention, and that there was also a publicly available computer program to find siRNAs for a given target. Tuschl (2) also provided ample guidance on the design of siRNA compounds. It is noted that the specification discloses at page 51 that a publicly available, prior art siRNA design tool was used to design SEQ ID NOS: 1 and 2.

Since the prior art taught inhibition of c-FLIP using an siRNA overlapping instant SEQ ID NO: 1, it is clear that the general region targeted by SEQ ID NO: 1 was of interest to those of ordinary skill. It would have been obvious to one of ordinary skill in the art at the time of the invention to synthesize other siRNAs in the immediate vicinity

in an attempt to optimize performance, and it would have been obvious to arrive at an siRNA comprising or consisting of instant SEQ ID NO: 1 through such routine optimization. It is noted that the methods taught in the prior art may not predict with 100% accuracy which siRNA compounds will inhibit c-FLIP, however, with the use of the prior art algorithms, basic teachings, and siRNA vendors, it would have been routine to make and test siRNA compounds targeted to c-FLIP in the region corresponding to SEQ ID NO: 1. The instant specification provides no evidence that the claimed siRNAs have unexpected properties. The invention as a whole would therefore have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 12/18/09 have been fully considered to the extent that they apply to the grounds of rejection set forth above, but they are not persuasive.

Applicant addresses the rejections over Siegmund, Wajant, and Xiang at pages 3 and 14 of the response.

Applicant notes that Wajant indicates that radiation and chemotherapy have significant side effects and are generally avoided if possible (paragraph 9), but that Wajant also taught that dsRNAs targeting c-FLIP can be used with chemotherapy and radiation (paragraph 64). Applicant judges the "the combination of dsRNAs against c-FLIP and a chemotherapeutic agent" to be "speculative at best" and concludes that the disclosure of Wajant cannot be considered to provide any suggestion specific

combinations of active agents that provide supra-additive effects. This is unpersuasive because the fact that Wajant indicated that chemotherapy causes side effects, and that such side-effects might be reduced through the use of siRNA, does not mean that one of ordinary skill would not consider using the two together in one method, as is clearly suggested by Wajant. Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. See MPEP 2123, citing *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994).

Applicant's assertion of supra-additive effects, previously relying for support on the specification at page 62, lines 17-28; page 63, lines 25-32; page 67, lines 5-20; and page 68, line 28 to page 69, line 10; and Figs. 11,B, 10C, 12A-C, and 13C is unpersuasive for the reasons of record. These passages allegedly provide evidence that the effects of FT (FLIP-targeted) siRNA combined with any of the chemotherapeutic drugs oxaliplatin, CPT-11, or 5-FU, resulted in synergistic effects on the amount of cells undergoing apoptosis. This is unpersuasive for at least two reasons. Evidence of unexpected results must be commensurate in scope with the claims (MPEP716.02(d)). In this case, one of the specification passages relied upon for support indicates that several FLIP- targeted siRNAs were tested, but that one potently down-regulated expression of both c-FLIP splice variants in HCT116p53^{+/+} cells at nanomolar concentrations. Thus it appears that a single siRNA was used in the experiments

relied on for evidence of unexpected results, but these passages do not disclose the identity of this siRNA. For example, it is unclear if the siRNA comprised either of SEQ ID NOS: 1 or 2. Furthermore, none of the rejected claims limits the identity of the c-FLIP inhibitor to siRNA. Note that claims 43, 44, and 48 embrace any RNAi agent comprising or consisting of SEQ ID NOS: 1 or 2. One of skill in the art could construe this as embracing miRNA, shRNA, and even antisense RNA alone. Claim 47 embraces any RNAi agent, and the rest of the claims under consideration embrace antisense or any c-FLIP inhibitor at all. Thus none of the claims under consideration is limited to whatever agent was used in the specification to produce the alleged unexpected results.

Applicant's assertion that one of ordinary skill would not have been motivated to combine TRAIL with other chemotherapeutic agents because such a combination might exert cytotoxic effects on normal tissue is unpersuasive in view of the fact that most, if not all, chemotherapeutic agents in clinical use at the time of the invention could exert cytotoxic effects on normal tissue. It was well known in the art prior to the time of the invention that chemotherapy frequently makes patients sick, but that its possible benefits are often estimated to outweigh its harmful effects. Furthermore, Applicant's response ignores the possible use of such a combination on cultured cells *in vitro* in the process of basic research into cancer cell physiology. Toxicity to normal cells would not be an issue in such a scenario.

Applicant argues at page 14 that claims 49-52 are distinguished over the combination of Siegmund, Wajant, and Xiang because a kit that does not include a death receptor binding member runs contrary to the basis provided by the Examiner for

combining the teachings of Siegmund and Xiang. This is unpersuasive for the reasons of record. The fact that the cited art renders obvious the combined use of c-FLIP siRNA, a death receptor binding member such as TRAIL, and a chemotherapeutic, does not mean that all compositions rendered obvious by the method must comprise TRAIL. One of ordinary skill in the art, aware of the cited references, could make compositions comprising one or more of these three agents, in any combination, for use in treating cancer. That is, one could combine the siRNA and the chemotherapeutic in one composition for use in the method of Siegmund or Wajant, and administer TRAIL separately. For example, as stated in the rejection, one would have been motivated to administer the siRNA and CPT-11 first in order to place the target tumor cells in a state in which they are maximally responsive to death receptor stimulation by CH-11 when it is administered separately later.

With regard to the rejection of claims 43, 44, and 48, Applicant asserts essentially that SEQ ID NO: 1 is comprised by the "FT siRNA" referred to in the specification. This assertion is supported by the Declaration of Dr. Daniel Longley, submitted 11/25/09, item 7. Applicant argues that instant SEQ ID NOS: 1 and 2 are not obvious in view of the cited art because they provide more potent RNAi agents than those cited in the prior art. Applicant relies for support on the Declaration of Dr. Daniel Longley, submitted 11/25/09. This is unpersuasive for several reasons. The experiments in the Declaration were performed on different cells, using a different transfection procedure, and a different detection assay than those used in the prior art reference (Siegmund). Siegmund delivered siRNAs to human epidermal KB cells by electroporation, and down-

regulation was assayed by fluorescence-activated cell sorting based on expression of a GFP-FLIP fusion protein. In contrast, the Declaration reports that colorectal cancer cells were transfected using oligofectamine transfection reagent, and expression was assayed by Western blot. It is not clear that these divergent experiments can provide a reliable comparison of the potency of the siRNAs in the claims and prior art, so it is unclear that the claimed siRNAs are statistically significantly more potent than those of the prior art. Note that it is Applicant's burden, when relying on evidence of unexpected results, to show that the results are of statistical and practical significance (MPEP 716.02(b)(I)). Note also that the evidence must be commensurate in scope with the claims. The evidence in the Declaration was obtained with siRNAs, whereas claims 43 and 48 are drawn to "RNAi agents" that comprise SEQ ID NO: 1 or 2. The breadth of the term "RNAi agents" includes dsRNAs other than the siRNAs of the Declaration. For example claims 43 and 48 read on hairpin RNAi reagents with antisense portions greater than 21 nucleotides that comprise both SEQ ID NO: 1 *and* the sequence disclosed by Siegmund. There is no evidence of record that such agents would be superior to the siRNAs of Siegmund. Note that claim 44 is drawn to an RNAi agent **consisting of** SEQ ID NO: 1 or SEQ ID NO: 2. This RNAi agent cannot be an siRNA as used in the Declaration, because siRNAs necessarily have sense and antisense strands, not just a single strand. It is not clear that delivery of an oligonucleotide consisting of SEQ ID NO: 1 or 2 would provide results similar to those presented in the Declaration. Accordingly the claimed subject matter is not commensurate in scope with the evidence presented. For these reasons the rejections are maintained.

Applicant addresses the rejection over Hyer, Uslu, Ni, and Tuschl at pages 15 and 16 of the response. Applicant asserts that if one were to consider testing the effect of CH-11 and Adriamycin/Etoposide in the presence of a c-FLIP inhibitor, that person would not have arrived at a result falling within the scope of the claims because adriamycin and etoposide are topoisomerase II inhibitors. This is unpersuasive for the reasons set forth in the rejection. The chemotherapeutics of Ni were found to be useful in combination with an apoptosis inducing method such that it would have been obvious to use them in combination with the CH-11 antibody and antisense of Hyer. In fact, it would have been obvious to use, in combination with the antisense and antibody of Hyer, any chemotherapeutic compound recognized as useful against prostate cancer cells. This is because it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, e.g. killing prostate tumor cells, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. See MPEP 2144.06(I).

For these reasons the rejections are maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Tracy Vivimore, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system

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/Richard Schnizer/

Primary Examiner, Art Unit 1635